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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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HAMRE, SCHUMANN, MUELLER & LARSON, P.C.
P.O. BOX 2902-0902
MINNEAPOLIS, MN 55402

EXAMINER	
MEAH, MOHAMMAD Y	

ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 06/13/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/526,026	YAMAOKA ET AL.	
	Examiner	Art Unit	
	Mohammad Meah	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 March 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-14* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-14* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *2/28/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

With the response filed 3/23/2006, the applicant elected without traverse Group I (claims 1-14) for further examination.

Election/Restriction

Applicant, on date 3/23/2006 elected without traverse Group I (claims 1-14) drawn to methods of purification of protein using liquid chromatography for examination. Groups II (claims 15-23) of election/restriction-office action of date 01/23/2006 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to nonelected Groups.

Priority

Acknowledgement is made of applicant's priority date based on application filing date of 08/20/2003 in Japan: Application No. pct/jpO3/10540and filing date 08/30/2002 in Japan: Application No. Japan 2002-253742.

Objections

Claim 3- is objected in recitation " target protein is provided by a glucose dehydrogenase", would be better stated - "target protein is a glucose dehydrogenase". **Appropriate correction is required.**

Claim 4- is objected in recitation " packing agent is provided by an ion-exchange gel ", would be better stated "packing agent is an ion-exchange gel". **Appropriate correction is required.**

Claim 11- are objected in recitation " microorganism belonging to the genus Burkholderia is provided by Burkholderia cepacia", would be better stated "microorganism is Burkholderia cepacia". **Appropriate correction is required.**

Claim 13- is objected in recitation " host microorganism is provided by Pseudomonas putida", would be better stated " host microorganism is Pseudomonas putida". **Appropriate correction is required.**

Claim 14- is objected in recitation " host microorganism is provided by E. coli", would be better stated " host microorganism is E. coli". **Appropriate correction is required.**

Claim 6- need the word "and" at the end of line 4 and " having" in line 6 should be "has". **Appropriate correction is required.**

Claim 8- " in the elution" in line 3 should be "during the elution". **Appropriate correction is required.**

and

Claim 12, --"for coding"- should be "encoding". **Appropriate correction is required.**

Claim Rejections

35 U.S.C 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

Claims 1-14 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1: " causing the packing agent to hold the target protein"- it is unclear what action this corresponds to?

Claims 2 and 3: "target protein contains an electron transfer protein" or "glucose dehydrogenase containing a protein---" - is confusing and unclear, how does one protein contain another protein? Did the applicant mean " contains an electron transfer protein domain or contains an electron transfer sub-unit "? or something else. Similar in claim 3 for "glucose dehydrogenase containing a protein---".

Claim 7: the recitation " hydroxy-cholate comprises a cholate"- is unclear what it means? A hydroxy-cholate inherently comprises a cholate.

Claim 12: " the protein active against glucose" lack antecedent basis

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-14 are rejected under U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to

reasonably convey to one skilled in the relevant art that the inventor at the time the application was filed, had possession of the claimed invention.

These claims are directed to methods of purification of a genus of proteins or genus of electron transfer proteins or genus of protein having glucose dehydrogenase (GDH) activity using liquid chromatography. The specification fails to describe in any fashion the physical and/or chemical properties of the claimed class of proteins or electron transfer proteins or GDH proteins. Claim 6 recite methods of purification of electron transfer protein of ~43 kDa mwt and GDH protein of ~60 kDa Mwt, without any specified structures encompass by the protein and claims 10-11 encompasses methods of using any liquid chromatography to purify any GDH from genus Burkholderia or any GDH from Burkholderia Cepacia (Burkholderia or Burkholderia Cepacia comprises GDH complexes comprising α, β and γ subunits (Inose et al. Biochi Biophys acta 2003, 1645, 133-138). Moreover the specification fails to describe any protein by identifying characteristics other than binding to liquid chromatography column and elution with cholate containing eluent. Since extent of binding to the liquid chromatography column and as well as elution by an eluent depends on the physical and chemical characteristics of the protein, given this lack of description of representative protein species encompassed by the genus of the claim, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicants were in possession of the claimed invention.

Claims 1-14 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of purification of GDH protein comprising α , β and γ subunit from Burkholderia Cepacia using hydrophobic interaction liquid chromatography or ion-exchange technique does not reasonably provide enablement for method of purification of any GDH protein from any source or any GDH from any Burkholderia or any GDH (α , β and γ) from Burkholderia Cepacia using any liquid chromatographic or ion-exchange technique. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

Claims 1-5 and 7-14 are so broad as to encompass methods of using any liquid chromatography or ion-exchange chromatography comprising cholate containing eluent to purify any protein, or any electron transfer protein or any GDH protein; while Claim 6 encompasses methods of using any liquid chromatography or ion-exchange chromatography comprising cholate containing eluent to purify electron transfer protein of ~43 kDa mwt and GDH protein of ~60 kDa Mwt and claims 10-11 encompasses methods of using any liquid chromatography to purify any GDH from genus Burkholderia or Burkholderia Cepacia (Burkholderia or Burkholderia Cepacia comprises GDH complexes comprising α, β and γ subunits (Inose et al. Biochi Biophys acta 2003, 1645, 133-138).The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of proteins,

or electron transfer proteins or GDH proteins and as well as broad class of liquid chromatography or ion-exchange chromatography broadly encompassed by the methods of the claims. Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. However, in this case the disclosure is limited to the nucleotide and encoded amino acid sequence of only two proteins.

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or multiple modifications, as encompassed by the instant claims, and the positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions.

The specification does not support the broad scope of the claims which encompass methods of using any liquid chromatography or ion-exchange chromatography comprising cholate containing eluent to purify any protein, or any electron transfer protein or any GDH protein, because the specification does

not establish: (A) regions of the protein structure which may be modified without effecting binding to the column material; (B) the general tolerance of polypeptide column binding activities to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any polypeptide residues with an expectation of obtaining the desired column binding function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including methods of using any liquid chromatography or ion-exchange chromatography comprising cholate containing eluent to purify any protein, or any electron transfer protein or any GDH protein. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of LTP polypeptides for the use in the claimed methods having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

CLAIM Rejection - 35 U.S.C 102

35 U.S.C 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1, 4 and 7-9 are rejected under 35 U.S.C. 102(b) as being anticipated by O'Riordan et al. (US Pat 5939536).

O'Riordan et al. teaches the purification of membrane-associated proteins using liquid chromatography including ion-exchange column wherein eluent is applied at constant gradient containing 0.5% to 2% cholate.

Claims 1-5, 7-9 are rejected under 35 U.S.C. 102(b) as being anticipated by Shimomura et al (Anal biochem 1986 vol 153, pp 126-131) and Imai et al (J. biochem 1976, vol 80, pp 267-76).

Shimomura et al teaches the purification of Cytochrome bc (a protein having electrone transfer and GDH unit) protein using liquid chromatography comprising phenyl-sepharose and ion exchange (DEAE (detergent exchange anion exchange) sepharose column, wherein eluent is applied at constant gradient containing 0.25% cholate.

Imai et al teaches the purification of cytochrome P450 (electron transfer protein and glucose reductase) protein using liquid chromatography protein

using liquid chromatography comprising aminooctyl-sepharose column, wherein eluent contain .15% Deoxy cholate 0.5% cholate.

CLAIM Rejection - 35 U.S.C 103a

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 6,10-14 are rejected under 35 U.S.C. 103(b) by Shimomura et al (Anal biochem 1986 vol 153, pp 126-131) in view of Inose et al. Biochemia biophysica acta 2003, 133-138).

Claims 6 and 10-14 are directed to the purification of GDH protein or electron transfer protein using liquid chromatography using eluent containing cholate wherein the GDH has a glucose dehydrogenase subunit of 60 kDa mwt and electron transfer subunit of 43 kDa mwt from microorganism Burkholderia or Burkholderia Cepacia or is produced by transformant such as P. Putida or E. coli.

Shimomura et al teaches the purification of Cytochrome bc (a protein having electrone transfer and GDH unit) protein using liquid chromatography comprising phenyl-sepharose and ion exchange (DEAE (detergent exchange anion exchange) sepharose column, wherein eluent is applied at constant gradient containing 0.25% cholate.

Inose teaches gene encoding GDH protein from microorganism Burkholderia Cepacia (Catalytic subunit mwt 60kDa and electron transfer subunit mwt 43 kDa) and GDH produced by transformant such as P. Putida or E. coli and also teaches the purification of said GDH protein by column and ion-exchange chromatography.

However Inose et al. do not teach the elution of said columns with a hydroxyl cholate gradient. Advantageous use of cholate as an eluent in hydrophobic-interaction liquid chromatography to purify Cy GDH proteins is well documented (Shimomura et al (Anal biochem 1986 vol 153, pp 126-131) and Imai et al (J. biochem 1976, vol 80, pp 267-76). As such it would have been obvious to one of ordinary skill in the art to obtain GDH protein from microorganism Burkholderia Cepacia and GDH produced by transformant such as P. Putida or E. coli taught by Inose and use the method of purification using liquid chromatography comprising phenyl-sepharose and ion exchange (DEAE (detergent exchange anion exchange) sepharose column, wherein eluent is applied at constant gradient containing 0.25% cholate as taught by Shimomura et al.

Applicant cannot rely upon the foreign priority papers to overcome this rejection because a translation of said papers has not been made of record in accordance with 37 CFR 1.55. See MPEP § 201.15.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mohammad Meah whose telephone number is 571-272-1261. The examiner can normally be reached on 8:30-5PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy can be reached on 571-272-0928. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Mohammad Younus Meah, PhD

Examiner, Art Unit 1652
Recombinant Enzymes, 3C31 Remsen Bld
400 Dulany Street, Alexandria, VA 22314

Telephone: 517-272-1261

REBECCA E. PRUTY
PRIMARY EXAMINER
GROUP ~~1800~~ 1600